metabolism modulating moiety binds to an extracellular protein.

65. (New) The method according to Claim 63, wherein said drug target is a protein.

66. (New) The method according to Claim 63, wherein said bifunctional molecule is administered as a pharmaceutical preparation.--

REMARKS

In view of the above amendments and the following remarks, the Examiner is respectfully requested to withdraw the rejections and allow Claims 16-17, 19 - 32 and newly added Claims 51 - 66, the only claims pending and under examination at this time.

Claims 16, 23 and 32 have been amended to remove the optional linker language and also to clarify that the free drug control includes the drug of the bifunctional molecule. In addition, new Claims 51 to 66 have been introduced, where these claims are the same as Claims 16-17 and 19-32, with the additional limitation that the bifunctional molecule includes a linker.

Attached hereto is a marked up version of the changes made to the claims by the current amendment. The attached page is captioned **"Version with Markings to Show Changes Made".** As can be seen from the above remarks and the attached copy of the marked up claims, no new matter has been introduced to the application by the above amendments. As such, the Examiner is respectfully requested to enter the above amendments.

Turning now to the rejections presented in the Office Action, Claims 16-32 were rejected under 35 U.S.C. § 112, 2nd ¶. In view of the above amendments which address the reasons for this rejection, it is respectfully submitted that this rejection may be

withdrawn.

Claims 16-32 were rejected under 35 U.S.C. 103(a) as being obvious over Briesewitz in view of Nygren and Pouletty. For the following reasons, this rejection may be withdrawn.

Section 102(a) reads: "A person shall be entitled to a patent unless (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent."

A printed publication cannot stand as a reference under §102(a), and therefore be used in a rejection under §103(a) in combination with other references, unless it describes the work of another. A prior patent or printed publication is not "prior art" if the disclosure is that of the Applicants' own work, until the end of the one year period afforded under §102(b), during which time an inventor is allowed to perfect, develop and apply for a patent on his invention and publish descriptions of it if he wishes.

Since the publication in this case occurred less than one year before the priority date of the Applicants' application, the disclosure comes within the scope of §102(a) only if the description is not of the Applicants' own work. Authorship of an article by itself does not raise a presumption of inventorship with respect to the subject matter disclosed in the article. Thus, co-authors may not be presumed to be coinventors merely from the fact of co-authorship (*see In re Katz*, 215 USPQ at 18).

Applicants have provided a Declaration made under 35 U.S.C. §1.132 describing the contributions of the co author Gregory Ray in the cited Briesewitz et al. paper. As stated in the declaration, Gregory Ray worked at the direction of the inventors of the presently named application.

In view of the above remarks and attached Declaration, the Applicants respectfully submit that the presently claimed invention is not obvious over Briesewitz et al., because Breisewitz cannot be used as a reference against the present application since it does not qualify as prior art to the present application under §102(a) or any other section of 102.

As such, the Applicants respectfully request withdrawal of this rejection of claims 16-32 under 35 U.S.C. §103(a).

In view of the above remarks, this application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issuance.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815.

Respectfully submitted,

BOZICEVIC, FIELD & FRANCIS LLP

Date: 10/28/2002

By: _____
Bret E. Field
Registration No. 37,620

encs: Declaration by Roger Briesewitz

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

16. (Once Amended) A method for modulating at least one pharmacokinetic property of a drug upon administration to a host, said method comprising:

administering to said host an effective amount of a bifunctional molecule of less than about 5000 daltons consisting of said drug or an active derivative thereof and a pharmacokinetic modulating moiety ~~optionally joined by a linking group~~, wherein said bifunctional molecule has at least one modulated pharmacokinetic property upon administration to said host as compared to a free drug control that comprises said drug;

whereby at least one pharmacokinetic property of said drug upon administration to said host is modulated as compared to a free drug control.

Cancel Claim 18.

23. (Once Amended) A method for modulating the half life of a drug upon administration to a host, said method comprising:

administering to said host an effective amount of a bifunctional molecule of less than about 5000 daltons consisting of said drug or an active derivative thereof and a half-life modulating moiety ~~optionally joined by a linking group~~, wherein said bifunctional molecule has a modified half-life upon administration to said host as compared to a free drug control that comprises said drug;

whereby the half life of said drug upon administration to said host is modulated as compared to a free drug control.

28. (Once Amended) A method for modulating the hepatic first-pass metabolism of a drug upon administration to a host, said method comprising:

administering to said host an effective amount of a bifunctional molecule of less than about 5000 daltons consisting of said drug or an active derivative thereof and a hepatic first-pass metabolism modulating moiety ~~optionally joined by a linking group~~, wherein said bifunctional molecule has a modified hepatic first-pass metabolism upon administration to said host as compared to a free drug control that comprises said drug;

whereby the hepatic first-pass metabolism of said drug upon administration to said host is modulated as compared to a free drug control.

Cancel Claims 33 to 50.

Please enter the following new claims:

--51. (New) A method for modulating at least one pharmacokinetic property of a drug upon administration to a host, said method comprising:

administering to said host an effective amount of a bifunctional molecule of less than about 5000 daltons consisting of said drug or an active derivative thereof and a pharmacokinetic modulating moiety joined by a linking group, wherein said bifunctional molecule has at least one modulated pharmacokinetic property upon administration to said host as compared to a free drug control that comprises said drug;

whereby at least one pharmacokinetic property of said drug upon administration to said host is modulated as compared to a free drug control.

52. (New) The method according to Claim 51, wherein said pharmacokinetic property is selected from the group consisting of half-life, hepatic first-pass metabolism, volume of distribution and degree of blood protein binding.

53. (New) The method according to Claim 51, wherein pharmacokinetic modulating moiety binds to an intracellular protein.

54. (New) The method according to Claim 51, wherein said pharmacokinetic modulating moiety binds to an extracellular protein.

55. (New) The method according to Claim 51, wherein said drug target is a protein.

56. (New) The method according to Claim 51, wherein said bifunctional molecule is administered as a pharmaceutical preparation.

57. (New) A method for modulating the half life of a drug upon administration to a host, said method comprising:

administering to said host an effective amount of a bifunctional molecule of less than about 5000 daltons consisting of said drug or an active derivative thereof and a half-life modulating moiety joined by a linking group, wherein said bifunctional molecule has a modified half-life upon administration to said host as compared to a free drug control that comprises said drug;

whereby the half life of said drug upon administration to said host is modulated as compared to a free drug control.

58. (New) The method according to Claim 57, wherein said half-life modulating moiety binds to an intracellular protein.

59. (New) The method according to Claim 57, wherein said half-life modulating moiety binds to an extracellular protein.

60. (New) The method according to Claim 57, wherein said drug target is a protein.

61. (New) The method according to Claim 57, wherein said bifunctional molecule is administered as a pharmaceutical preparation.

62. (New) A method for modulating the hepatic first-pass metabolism of a drug upon administration to a host, said method comprising:

administering to said host an effective amount of a bifunctional molecule of less than about 5000 daltons consisting of said drug or an active derivative thereof and a hepatic first-pass metabolism modulating moiety joined by a linking group, wherein said bifunctional molecule has a modified hepatic first-pass metabolism upon administration to said host as compared to a free drug control that comprises said drug;

whereby the hepatic first-pass metabolism of said drug upon administration to said host is modulated as compared to a free drug control.

63. (New) The method according to Claim 62, wherein said hepatic first-pass metabolism modulating moiety binds to an intracellular protein.

64. (New) The method according to Claim 63, wherein said hepatic first-pass metabolism modulating moiety binds to an extracellular protein.

65. (New) The method according to Claim 63, wherein said drug target is a protein.

66. (New) The method according to Claim 63, wherein said bifunctional molecule is administered as a pharmaceutical preparation.--